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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,667	07/28/2000	David Putnam	1668714	3663

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/628,667	PUTNAM ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *136,140,145-147,150,152-155,161-163 and 166-180* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136,140,145-147,150,152-155,161-163 and 166-180* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' 4/27/06 response has been entered. Claims 136-156 and 158-177 were pending in the application. Applicants "added new claims 179 and 180, canceled claims 137-139, 141-144, 148, 149, 151, 156-160, 164, and 165 and amended claims 136 and 155" (e.g., see 4/27/06 Response, page 9, paragraph 1; see also newly amended claims). Furthermore, Applicants state that these claims "read on the elected invention" (e.g., see 4/27/06 Response, page 9, paragraph 1). Therefore, claims 136, 140, 145-147, 150, 152-155, 161-163, and 166-180 are currently pending and examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Priority

2. Applicants' claim for domestic priority under 35 U.S.C. § 119(e) and/or § 120 is acknowledged. However, Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 119(e) and/or 120 as follows:

This application is a CIP of 09/540,462 (referred to herein as '462) filed 03/31/2000, now abandoned, which is a continuation of claims benefit of 60/127,755 (referred to herein as'755)

filed 04/05/1999. However, both application fail to provide adequate support under 35 U.S.C. § 112, first paragraph for the claimed invention as follows:

> (A) For ***claims 136, 152-155, 168-170, 179 and 180 (and all dependent claims)***, both applications fail to provide support for the currently claimed "data mining algorithms." For example, the '462 application only provides support for "two types of Infomatics ... One is system automation and control software that enables the integrated set of manipulations to occur and track the process flow [i.e., does not constitute data mining] ... A second is scientific derivatization which collects and stores data to enable further development and design of formulations, including identification of complex interactions between the actives and excipients, and identification of lead formulations" (e.g., see '462, paragraph bridging pages 22 and 23; see also 25, line 9 wherein use of the "MATLAB" program is disclosed). Data mining is a broad term that would encompass more than just the "identification of complex interactions between the actives and excipients" and" identification of lead formula" and/or use of MatLab program. Data mining would encompass every conceivable relationship (e.g., see Wikipedia, the Free Encyclopedia. data mining. Retrieved at http://en.wiktionary.org/wiki/Data_mining on October 14, 2006, page 1, "a technique for searching large-scale databases for patterns; used mainly to find previously unknown correlations between variables that may be commercially useful") using many different algorithms. In addition, the '755 application does not even disclose "informatics" at all. The '755 application merely states, "[t]hese systems are connected to computers for analysis of the data using appropriate software and data sets" (e.g., see '755, last page before claims, line 10 and 11). In addition, the '755 application fails to disclose the "MatLab" program. Therefore, the '755 application provides no support for "data mining" whatsoever. In support of this position the Examiner notes that neither application discloses any of the programs for conducting data mining such as SPOTFIRE, MATLAB, STATISCA, etc. as disclosed in the present application (e.g., see specification, page 37, paragraph 2). Furthermore, both applications fail to disclose a central server and/or data base.
> (B) For ***claims 147 and 163 (and all dependent claims)***, both applications fail to provide support for sample volumes between 150 and 200 µl
> (C) For ***claims 171 and 172 (and all dependent claims)***, both applications fail to provide support for each sample comprises at least three excipients selected form the group consisting of: acidulents; solubilizing components; absorbents, alkalizing components; anticaking components; antimicrobial components; antioxidants; binders; buffering components; chelating components; coating components; controlled release vehicles; detergents; emollients; emulsifying components; flavoring components; humectants; lubricants; solvents; stabilizing components; tonicity components; binders; fillers; and mixtures thereof.
> (D) For ***claims 155 and 180*** (and all dependent claims), the '755 application fails to provide support for monitoring "synergistic" interactions.

If applicant believes this assessment is in error, applicant must disclose where in the specification support for these limitations can be found. Therefore the filing date of the instant application is deemed to be its actual filing date, **July 28, 2000**.

Withdrawn Objections/Rejections

3. The Sharma rejection under 35 U.S.C. § 103(a) is hereby withdrawn in favor of a new Sharma rejection including Rasnow et al. in addition to the previously cited references.

New Rejections and/or Objections

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 140 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 140 depends on canceled claim 139 (i.e., a non-existent claim) and it is thus unclear what subject matter the appellant intended to cover. Furthermore, there is no antecedent basis for "the method of claim 139" or "the component in common" as set forth in line 1 of the claim.

Claim Rejections - 35 USC § 103

5. Claims 136, 140, 145-147, 150, 152-155, 161-163 and 166-180 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma et al. (Sharma, U. S.; Balasubramanian, S. V.; Straubinger, R. M. "Pharmaceutical and Physical Properties of Paclitaxel (Taxol) Complexes with Cyclodextrins" *J. Pham. Sci.* **1995**, *84*, *10*, 1223-1230) and Merritt (Merritt, A. T. "Uptake of new technology in lead optimization for drug discovery" **1998** DDT, 3(11), 505-510) and

Saneii et al. (U.S. Patent No. 5,746,982) (Date of Patent is **May 5, 1998**) and Wang et al. (Wang, T.; Zeng, L.; Strader, T.; Burton, L.; Kassel, D. B. "A New Ultra-high Throughput Method for Characterizing Combinatorial Libraries Incorporating a Multiple Probe Autosampler Coupled with Flow Injection mass Spectrometry Analysis" *Rapid Commun. mass Spectrom.* **1998** *12*, 1123-1129) and Lipinski et al. (Lipinski, C. A.; Lombardo, F.; Dominy, B. W.; Feeney, P. J. "Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings" Advanced Drug Delivery Reviews **1997**, *23*, 3-25) and Rasnow et al. (Rasnow et al., "Matlab for Laboratory Automation" LabAutomation'99 Final conference Program January 30-February 3, 1999, pages 255 and 256).

For ***claims 136, 155 and 178***, Sharma et al. (see entire document) teach a method for analyzing the increase in solubility of paclitaxel as a result of its interactions with a library of cyclodextrins, which reads on the claimed invention (e.g., see Sharma et al., abstract). For example, Sharma et al. disclose **(a)(1)** a library of samples that contain a component-in-common and one or more additional components (e.g., see Sharma et al., Table 1 wherein component-in-common = Paclitaxel and additional component = cyclodextrins). In addition, Sharma et al. disclose varying the identity of the one or more additional components or varying in the ratio of the volume of component-in-common to the volume of the one ore more additional components (e.g., see Sharma et al., Table 1 wherein the identity is varied, such as HEβ, HPβ, DMβ, etc.). Sharma et al. also disclose **(b)** testing each sample for a property to generate a data set (e.g., see Table 1, showing amount of Paclitaxel dissolved; see also figure 1; see also figure 2; see also Experimental section). Sharma et al. also disclose **(c)** analyzing the data set to measure or detect an

interaction between components of the sample formulations, said interaction being increased solubility of the component-in-common (e.g., see Table 1, disclosing solubility "enhancement" factor that results from interaction of Paclitaxel with cyclodextrin). For claim 155, Sharma et al. also disclose the use of synergistic interactions between different cyclodextrins to achieve greater solubility with a lower renal and hemolytic toxicity (e.g., see page 1229, last paragraph).

For ***claims 140, 149, 173 and 174***, Sharma et al. disclose Applicants' elected Paclitaxel therapeutic pharmaceutical in a liquid "dissolved" form (e.g., see Sharma et al., abstract).

For ***claims 145, 146, 161, 162***, Sharma et al. disclose the use of samples less than 100 ng of sample (e.g., see Sharma et al., Table 1; see also Lipinski et al. and Merritt references below). In addition, the Examiner notes "the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955). Also note that optimization of process steps, especially with respect to numbers of samples analyzed, numbers of substrate regions and quantity of sample used is within the routine skill of the art. *In re Burhans*, 154 F.2d 690, 69 USPQ330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results). With respect to the repetition of steps (i.e. number of samples analyzed or number of substrate regions), see *In re Harza*, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. With

respect to the quantity of sample used, it is clear that the mere scaling up of a prior art process capable of being scaled up would not establish patentability in a claim to an old process so scaled *In re Rinehart*, 531 F.2d. 1048, 189 U.S.P.Q. 143 (C.C.P.A. 1976).

For ***claim 167***, Sharma et al. disclose the "optimization" of formulations (e.g., see Table I showing enhancement factor of 99000 for 50%DMβ; see also 60%HPβ, which has an enhancement factor of 10000 compared to only 2140 for 50% HPβ).

For ***claims 171 and 172***, Sharma et al. disclose at least three "solubilizing" excipients (e.g., see Sharma et al., page 1229, column 2, paragraph 1 wherein a mixed alkyl, hydroxyalkyl and carboxyalkyl ether derivatives are disclosed).

The prior art teachings of Sharma et al. differ from the claimed invention as follows:

For ***claims 136, 152-155, 168-170, 178-180***, Sharma et al. fail to disclose **(a)(2)** samples at separate sites in the array or located at separate wells in the array. Sharma et al. also fail to disclose **(a)(3)** an array comprising at least 1,000 different samples. Furthermore, Sharma et al. fail to disclose **(a)(4)** preparation of an array via an automated system that adds and mixes the components of each sample under software control. Sharma et al. also fail to disclose the use of "data mining algorithms."

For ***claim 147 and 163***, Sharma et al. fail to disclose an array wherein each sample of the array has a total volume between 150 and 200 µl.

For ***claim 166***, Sharma et al. fail to disclose 1000 formulations per day.

For ***claims 175-177***, Sharma et al. fail to disclose use of UV spectrometer.

However, the combined references of Merritt, Rasnow et al., Saneii et al., Wang

et al., and Lipinski et al. teach the following limitations that are deficient in Sharma et al.:

For ***claims 136, 152-155, 168-170, 178-180***, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. (see entire document) teach **(a)(2)** the use of separate wells on an array (e.g., see Merritt, page 1998, column 2, paragraph 1 wherein a microtiter plate is disclosed; see also figure 1). Furthermore, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. teach **(a)(3)** the use of over one million samples (e.g., see Merritt, page 1998, column 2, paragraph 1). In addition, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. teach **(a)(4)** the use of automated system that adds and mixes the components of each sample under software control (e.g., see page 1998, column 1, last paragraph wherein Applicants' elected Tecan 5072 Robotic Sample Processor is disclosed; see also figure 1; see also page 507, "Who need a Computer" section). In addition, the Examiner notes "the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955). Also note that optimization of process steps, especially with respect to numbers of samples analyzed or numbers of substrate regions is within the routine skill of the art. *In re Burhans*, 154 F.2d 690, 69 USPQ330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results). With respect to the repetition of steps (i.e. number of samples analyzed or number of substrate regions), see *In re Harza*, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance

unless a new and unexpected result is produced. In addition, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. disclose the use of "data mining algorithms" (e.g., see Lipinski et al., section 2.3; see also section 3; see also section 4; see also Rasnow et al., page 255, disclosing MATLAB "data mining" software including "neural networks" toolboxes).

For ***claims 145-147 and 161-163***, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. disclose 100 ng of sample (e.g., see Lipinski et al., section 2.17, especially, page 15, column 2, last paragraph showing < 5μg/ml for 2.5 ml volume = ~ 12.5 μg; see also Merritt, figure 1). The combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. also disclose the use of a total volume between 150 and 200 μl (e.g., see Merritt, page 506, paragraph bridging columns 1 and 2; see also figure 1).

For ***claim 166***, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. disclose 1000 formulations per day (e.g, see Merritt, page 506, column 2, paragraph 1, "... over a period of two years the equipment was used to prepare about one million compounds for assay" i.e., 1,000,000/2 × 365 = 1369/day). In addition, the Examiner notes "the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA1955). Also note that optimization of process steps, especially with respect to numbers of samples analyzed or numbers of substrate regions is within the routine skill of the art. With respect to the repetition of steps (i.e. number of samples analyzed or number of

substrate regions), see *In re Harza*, (274 F.2d 669, 124 USPQ 378 (CCPA 1960)) where the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced.

For ***claims 175-177***, the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. disclose the use of UV spectrometer (e.g., see Lipinski et al., section 2.18).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to use the commercially available robotic liquid handling devices disclosed by the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. to prepare and/or analyze the library of Pacltaxel/Cyclodextrin pharmaceutical drug formulations because the commercially available liquid handling devices disclosed by the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. were explicitly designed for this purpose (e.g., see Merritt, column 1, paragraph 1, "The introduction of automation and increasing levels of miniaturization in the high-throughput screening (HTS) arena at the start of the 1990s provided the impetus for the development of combinatorial chemistry in drug discovery"; see also page 510, column 1, paragraph 1, "These techniques [automated HTS] have been embraced by medicinal chemists, and are now applied as part of the wide range of approaches available to tackle the discovery and development of new drugs), which would encompass the "development" of the Paclitaxel drugs disclosed by Sharma et al. Furthermore, one of ordinary skill in the art would have been motivated to use the commercially available liquid handling devices as disclosed by the combined references

of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. because according to the combined references these automated systems have numerous advantages for conveniently and reproducibly screening large numbers of samples with optimal controls by the practitioner to increase the speed and/or reduce the costs via, for example, the use of small sample volumes and fast computer automation (e.g., see Merritt, page 507, column 2, last paragraph, "... instead of developing a single piece of equipment to perform all the functions of the synthetic process we had separated the functions into stand-alone modules. This allowed more-flexible equipment scheduling and use"; see also Wang et al., paragraph bridging pages 1125 and 1126, "Our ease of acquiring FIA-MS data on samples 8 in a time of less than one minute suggested the possibility of processing an entire microtiter plate in less than 10 minutes (providing at least a four-to-five-fold speed advantage over existing technologies). However, to maintain this speed advantage, it was critical to develop tools to facilitate automated data acquisition and data processing ... To permit autosampling of eight samples at a time, an Excel ^{TM} macro was used to automatically convert a text file, containing information about the expected products in each well of a microtiter plate, into a format amenable to automated data acquisition and data processing of eight samples at a time"). In addition, this automation is particularly important for solubility studies (e.g., see Lipinski et al., section 5, especially page 23, column 2, especially first full paragraph, "... we believe a competitive advantage accrues to the organization that can identify compound sets likely to give leads more easily converted to orally active drugs [i.e., water soluble]"; see also section 2.15, "High throughput screening hits, calculations and solubility measurements";

see also abstract), which would encompass the solubility studies disclosed by Sharma et al. Furthermore, Rasnow et al. state that "data mining" programs like Matlab are essential for lab automation stating, "As lab automation matures, tasks are becomibn more complex than justmoving robotics between points and throwing relays. Integrating apparatuscontrol, data and image acquisition, and data analysis promises to increase the utility of lab automation" (e.g., see Rasnow et al., page 255) (emphasis added). Finally, one of ordinary skill in the art would reasonably have expected to be successful because the combined references of Merritt, Rasnow et al., Saneii et al., Wang et al., and Lipinski et al. disclose that automated robotic liquid sample handling devices are compatible with, and routinely used in, a wide variety of chemical applications and are especially useful in the pharmaceutical industry (e.g., see Merritt, page 510, column 1, last paragraph, "These techniques have been embraced by medicinal chemists, and are now applied as part of the wide range of approaches available e to tackle the discovery and development of new drugs"; see also Saneii et al., last two paragraphs, "From the foregoing it will be seen that the apparatus of the present invention is highly flexible and is capable of synthesizing a variety of compounds in a single setup or producing a larger quantity of a single compound in the wells").

Response

6. To the extent that Applicants' previous arguments could be applied against the newly cited rejection the following comments are noted:

Applicants argue, "The Office Action indicates that a method that utilizes "Spotfire software" has been searched and was not found in the prior art. Accordingly, Applicant has now amended the claims to recite the use of "data mining algorithms" (e.g., Spotfire software) in the claimed method steps to place the subject application in condition for allowance and conclude prosecution of this application. " (e.g., see 4/27/06 Response, page 9, last full paragraph).

This is not found persuasive for the following reasons:

The Office only indicated that "Spotfire" was not found, not the broader "data mining algorithms" that are currently claimed (e.g., see Final Office Action, page 9, paragraph 2, "For claims 152-154 and 168-1 70, the combined references of Merritt, Saneii et al., Wang et al., and Lipinski et al. disclose the use of data mining algorithms (e.g., see Lipinski et al., section 2.3; see also section 3; see also section 4)"; see also the newly cited Rasnow et al. disclosing the use of "MatLab" software). Therefore, Applicants' arguments are moot.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
October 15, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER